

Heart Rate Variability and Its Association with Mortality in Prehospital Trauma Patients

William H. Cooke, PhD, Jose Salinas, PhD, Victor A. Convertino, PhD, David A. Ludwig, PhD, Denise Hinds, RN, James H. Duke, MD, Fredrick A. Moore, MD, and John B. Holcomb, MD

Background: Accurate prehospital triage of trauma patients is difficult, especially in mass casualty situations. Accordingly, the U.S. Military has initiated a program directed toward improving noninvasive prehospital triage algorithms based on available physiologic data. The purpose of this study was to assess heart rate variability and its association with mortality in prehospital trauma patients.

Methods: Trauma patients without significant head injury requiring helicopter transport were identified from a retrospective research database. An equal number, unmatched sample of patients who lived were compared with those who died ($n = 15$ per group). All patients were transported to a single Level I urban trauma center. The primary independent variable was mortality. Patients with Abbreviated Injury Scale head scores >2 were excluded from the analysis, so that the effects seen were based on hemorrhagic shock. Age, sex, Glasgow Coma

Scale score (GCS), blood pressure, pulse pressure, pulse, intubation rate, SpO_2 , mechanism of injury, transport time, and time of death after admission were recorded. R-waves from the first available 120 seconds of usable data were detected from normal electrocardiograms and heart rate variability was assessed.

Results: Patients who died demonstrated a lower GCS (7.9 ± 1.4 versus 14.4 ± 0.2 ; $p = 0.0001$) and higher intubation rate (53% of patients who died versus 0% patients who lived). Pulse rate, arterial pressure, and SpO_2 were not distinguishable statistically between groups ($p = 0.08$), but pulse pressure was lower in patients who died (39 ± 3 versus 50 ± 2 mm Hg; $p = 0.01$). Compared with patients who lived, those who died had lower normalized low-frequency (LF) power (42 ± 6 versus 62 ± 4 LF_{nu}; $p = 0.009$), higher high-frequency (HF) power (42 ± 3 versus 32 ± 3 HF_{nu}; $p = 0.04$) and higher HF-to-LF ratio (144 ± 30 versus $62 \pm$

11_{nu} ; $p = 0.01$). With absolute HF/LF adjusted for GCS, the intergroup variance accounted for by HF/LF was reduced to 6% ($p = 0.16$).

Conclusions: Analysis of heart rate variability provides insight into adequacy of autonomic compensation to severe trauma. In our cohort of trauma patients, low pulse pressures coupled with relatively higher parasympathetic than sympathetic modulation characterized and separated patients who died versus patients who survived traumatic injuries when standard physiologic measurements are not different. These data do not suggest advantages of heart rate variability analysis over GCS scores, but suggest future possibilities for remote noninvasive triage of casualties when GCS scores are unattainable.

Key Words: Power spectral analysis, Trauma Vitals Database, Autonomic balance.

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Traumatic injury is the leading cause of death from ages 1 to 44 years, and approximately 40% of patients suffering fatal traumatic injuries die before they reach a hospital.¹ In the military environment, this number can be up to 90%.² In civilian trauma patients, arterial pressure, heart rate, arterial hemoglobin saturation, and mentation are routinely mon-

itored during transport; when abnormal, they clearly are related to mortality and provoke rapid evacuation and immediate interventions. In the military or civilian mass casualty event, this level of monitoring may be difficult. Additionally, these physiologic changes are relatively late secondary (decompensated physiologic responses), rather than primary, manifestations of hemorrhagic shock, and as such may not provide the first responder with adequate information regarding triage categories, evacuation priority, and required interventions.

Autonomic neural modulation of the circulation is the primary compensatory response to traumatic hemorrhage, and patients with adequate autonomic responses are better able to maintain peripheral resistance and arterial pressure compared with those patients whose autonomic responses are not adequate. We have shown that estimates of autonomic activity change as direct inverse functions of the magnitude of negative pressure applied to the lower body of human volunteers.³ Lower-body negative pressure is useful as an experimental procedure to induce controlled, progressive reductions of central blood volume and resulting cardiovascular

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From the Department of Health and Kinesiology, The University of Texas at San Antonio, San Antonio, Texas (W.H.C.); U.S. Army Institute of Surgical Research (W.H.C., J.S., V.A.C., J.B.H.), Fort Sam Houston, Texas; the Department of Pediatrics (D.A.L.), Georgia Prevention Institute, Medical College of Georgia, Augusta, Georgia; and the Department of Surgery (D.N., J.H.D., F.A.M.), University of Texas Health Sciences Center, Houston, Texas.

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Address for reprints: William H. Cooke, PhD, Department of Health and Kinesiology, The University of Texas at San Antonio, 6900 North Loop 1604 West, San Antonio, Texas 78249.

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compensations similar to actual hemorrhage.⁴ Thus, it is reasonable to propose that monitoring of autonomic function in trauma patients may provide early information to the first responder not contained in other measurements of hemodynamic stability.

Power spectral analysis has emerged as a useful noninvasive tool using simple electrocardiogram (ECG) recordings for quantifying relative parasympathetic and sympathetic activities by separating R–R interval oscillations into their high-frequency (HF; 0.15 to 0.4 Hz) and low-frequency (LF; 0.05 to 0.15 Hz) components. Analysis of heart rate variability provides quantitative estimates of autonomic neural activity⁵ and may have prognostic value for hospitalized trauma patients.^{6–8}

For example, in a large cohort of both cardiac and noncardiac patients ($n \cong 740$), Winchell and Hoyt⁷ estimated relative parasympathetic and sympathetic activities by applying power spectral analysis to cardiac interbeat intervals. They concluded that survival was associated with low parasympathetic and high sympathetic predominance, and death was associated with high parasympathetic and low sympathetic predominance. Heart rate variability analysis may characterize adequacy of autonomic compensation to an acute traumatic event, but to our knowledge, heart rate variability analysis has not been applied to trauma patients in a prehospital setting. The purpose of this study was to test the hypothesis that mortality in prehospital trauma patients is associated with higher parasympathetic and lower sympathetic autonomic activity as estimated from analysis of heart rate variability. We introduce the concept that estimates of autonomic function may allow for the separation and classification of trauma patients who may appear normal utilizing standard physiologic assessments,⁹ but who will ultimately die from their injuries.

PATIENTS AND METHODS

This study was approved by the Institutional Review Board of the University of Texas Health Science Center, Houston, Texas, and the Research Review Committee of the U.S. Army Institute of Surgical Research and the Brooke Army Medical Center Institutional Review Board, Fort Sam Houston, Texas. Patients were enrolled for this study using the Trauma Vitals database system developed by the U.S. Army Institute of Surgical Research. The system provides a data warehousing capability for storing and correlating prehospital patient data from incident pickup until delivery via Life Flight helicopter to Memorial Hermann Hospital, a regional Level I trauma center in Houston. Life Flight utilizes standard treatment protocols to guide onboard interventions. From a total patient population of 914, we identified 93 patients who died from their injuries (~10%). Of these patients who died, we excluded 66 patients because they had either incomplete data, no ECG recorded, or had an Abbreviated Injury Score (AIS) head score >2. Of the remaining 26 patients who met our criteria for inclusion, 11 were excluded

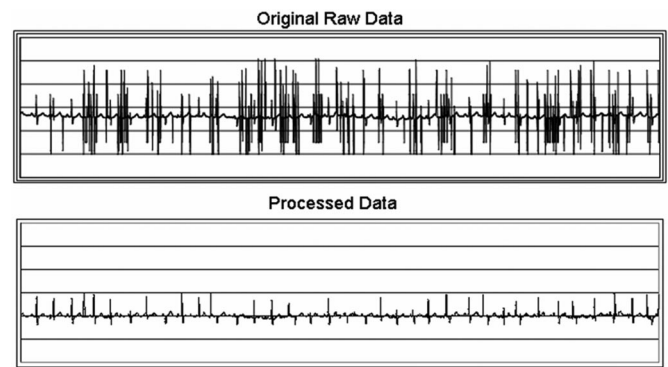


Fig. 1. Raw ECG data obtained directly from the ProPac 206EL is shown in the upper panel (original raw data). The same data are shown in the lower panel (processed data) after extensive filtering established stable baselines and removed noise spikes and movement artifacts from the signal.

based on the very poor quality of their ECG signal. We were therefore able to obtain analyzable data from 15 patients who died from their injuries. We chose for analysis an equal number of 15 patients with similar exclusion criteria who lived. For this exploratory study, we did not attempt to match patient groups for age, sex, or some other parameter.

Data Collection

Data were collected using both an automated data collection device for capturing values generated by the on-board vital signs monitor and through the standard run sheet for every patient. Vital signs, Glasgow Coma Scale score (GCS), age, sex, mechanism of injury, and incident demographics were recorded. Arterial pressures were measured automatically and recorded every 3 minutes. Arterial pressure and SpO₂ (pulse oximetry) data presented in this report were taken within 3 minutes of the ECG dataset used for heart rate variability analysis. ECG data were collected with an iPAQ (Talla-tech RPDA, Tallahassee, FL) personal digital assistant interfaced with a ProPac 206EL vital signs monitor (WelchAllyn, Beaverton, OR) and recorded with a sampling frequency of 182 Hz. All descriptive data including clinical outcomes were recorded prospectively by a single research nurse.

Heart Rate Variability Analyses

ECG data were extracted from the Trauma Vitals database, and then manually filtered and cleaned with customized software to remove noise artifacts. An example of the magnitude of data filtering required for one representative patient is shown in Figure 1.

Filtered and cleaned ECG signals were analyzed with a commercially-available software analysis package (WinCPRS, Absolute Aliens, Turku, Finland). We identified the first 2 minutes of continuous data for each patient, and these sections were considered valid if data were clean enough to identify with certainty individual R waves for each

Table 1 Patient Characteristics

Variable	Died	Lived	F Ratio	p Value
n	15	15		
Age (years)	43 ± 2	35 ± 3	2.2	0.15
Sex				
Male	13	13		
Female	2	2		
Blunt injury (%)	73	60	0.6*	0.45
Glasgow Coma Scale score	7.9 ± 1.4	14.4 ± 0.2	19.8	0.0001
Time to death (hours)	153 ± 59			
Transport time (minutes)	15.3 ± 1.8	12.4 ± 1.5	1.8	0.19
Estimated time after injury to data collection (minutes)	42.2 ± 3.6	49.2 ± 4.1 [†]	1.5	0.22
Intubated (%)	53	0	10.9*	0.001

Values are means ± SE.

*Estimated by χ^2 test.

[†]n = 14.

cardiac cycle. Data sets including noisy ECGs, ectopic beats, or “spikes” that could not be identified clearly by their position in the cardiac cycle were excluded from analysis and these patients were not included in the final dataset: a total of 11 of 26 patients who died and met our inclusion criteria were excluded from analysis due to these criteria for clean ECG signals.

Heart rate variability was assessed in the time domain by calculating the standard deviation (SD) of average R–R intervals (RRISD), the square root of the mean squared differences of successive R–R intervals (RMSSD), and the percentage of adjacent normal R–R intervals that varied by at least 50 ms or more (pNN50). Heart rate variability was assessed in the frequency domain from R–R interval spectral power. To calculate power spectra, consecutive R–R intervals were made equidistant by spline interpolating and resampling at 5 Hz. Data then were passed through a low-pass impulse response filter with a cutoff frequency of 0.5 Hz. Data sets were analyzed in the frequency domain using a Fourier transform with a Hanning window as described previously.^{9–13} Heart rate variability was quantified by calculating the total integrated area under the power spectrum (Tot: 0.05–0.4 Hz). Integrated areas were also separated into HF (0.15–0.4 Hz) and LF (0.05–0.15 Hz) bands. To compare power spectra more accurately from different patients who may vary widely in total power, we normalized our data in the LF (LF_{nu}) and HF (HF_{nu}) ranges by dividing integrated LF and HF spectra by the total power (minus oscillations occurring below 0.05 Hz) and multiplying this value by 100.^{14,15} We took the quotient of HF/LF as a global index of changes in autonomic balance.¹⁵

Statistical Analysis

We analyzed our data with commercial statistical software (SAS Institute, Cary, NC). The primary independent variable for univariate analyses was mortality. Differences between the means of each dependent variable were tested with a one-way ANOVA with comparisons between groups

(patients who died versus patients who lived). We also analyzed our data further using logistic regression. For the multivariate phase, the lived/died grouping was modeled as the dependent effect. The variable HF/LF was found to contain all of the relevant information from each of the redundant frequency-domain calculations performed for the univariate analyses. Logistic regression was used to test for the unique effect of HF/LF after controlling for each of three covariates (age, sex, and GCS score). To aid in the interpretation of the results, adjusted group means were calculated via inverse prediction of the logistic model. Exact *p* values were calculated for all statistical tests and reflect the probability of obtaining the observed or greater effect given only random departure from the assumption of no effects. All data are expressed as means ± standard errors unless specified otherwise.

RESULTS

Subject characteristics, classifications, and descriptive data are displayed in Table 1. Injury mechanisms (blunt or penetrating) were similar between groups. Transport time and the estimated time after incident occurrence until admission to the emergency department were not distinguishable statistically between patient populations (Table 1). Median time to death after injury for patients who died was 9.5 hours. Patients who died had lower GCS scores compared with patients who lived. Intubation rate was 53% for patients who died; no patients who lived were intubated. No patient who died had an AIS head score >1.

Electrocardiograms obtained during transport on the Life Flight helicopter were, as expected, consistently noisy and contained numerous movement artifacts. To obtain a sample size appropriate for rigorous statistical analysis, we determined a priori, based on the availability of clean ECG signals from which R waves were clearly distinguishable, that analyses would be done on 2-minute data sets. Two minutes is sufficient to interpret oscillations occurring within the frequency band of interest (0.05–0.4 Hz).¹⁴

Table 2 Time Domain Results for Patients Who Died and Patients Who Survived Traumatic Injuries during Transport on a Life Flight Helicopter

Variable	Died	Lived	F Ratio	p value
n	15	15		
RRI (ms)	605 ± 37	712 ± 46	3.3	0.08
RRISD (ms)	58 ± 14.6	47 ± 7	0.45	0.51
RMSSD (ms)	53 ± 12	43 ± 7	0.47	0.50
pNN50 (%)	13 ± 5	13 ± 4	0.0	0.96
Heart rate (bpm)	105 ± 6	90 ± 6	3.2	0.08
SpO ₂ (%)	90 ± 6*	98 ± 0.9†	2.3	0.14

Values are means ± SE.

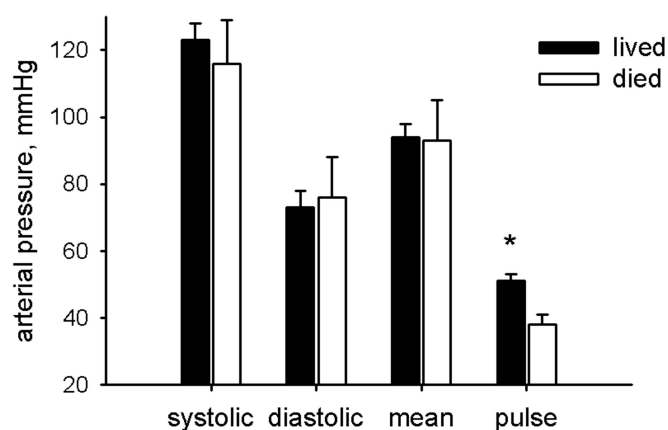
*n = 9.

†n = 12.

RRI, R-R interval; RRISD, R-R interval standard deviation; RMSSD, the square root of the mean squared differences of successive R-R intervals; pNN50, the percentage of adjacent normal R-R intervals that vary by at least 50 ms or more; SpO₂, arterial oxygen saturation.

Numerical results derived from time-domain analyses are shown in Table 2. Heart rates and R-R intervals, as well as global measures of heart rate variability including RRISD, RMSSD, and pNN50 were indistinguishable statistically between the two patient groups. SpO₂ values were unstable and inconsistent for nine patients. Values were determined to be stable and reliable when pulse rates from the pulse oximeter matched pulse rates from the radial pulse. These SpO₂ values were taken within 3 minutes of the ECG data used to assess heart rate variability. With these criteria, we analyzed SpO₂ from nine patients who died and 12 patients who lived, and found that SpO₂ was similar between groups. Patient groups had similar systolic, diastolic, and mean arterial pressures, but pulse pressures were lower (39 ± 3 versus 50 ± 2 mm Hg; $p = 0.01$) in patients who died compared with patients who lived (Fig. 2).

Table 3 shows results from frequency-domain analyses. Total power, HF and LF power were not different statistically

**Fig. 2.** Arterial pressures and pulse pressures are shown for 13 patients who died and 15 patients who survived traumatic injuries requiring transport to a level one trauma center. * $p = 0.001$.**Table 3** Frequency Domain Results for Patients Who Died and Patients Who Survived Traumatic Injuries during Transport on a Life Flight Helicopter

Variable	Died	Lived	F Ratio	p Value
n	15	15		
HF (ms ²)	635 ± 434	457 ± 163	0.15	0.70
LF (ms ²)	618 ± 322	833 ± 272	0.26	0.61
Tot (ms ²)	1253 ± 750	1290 ± 411	0.0	0.96
LF/HF	240 ± 147	250 ± 46	0.0	0.95
HF/LF	174 ± 32	65 ± 12	10.8	0.003
HF _{nu}	42 ± 3	32 ± 3	4.3	0.04
LF _{nu}	42 ± 6	62 ± 4	7.7	0.009
HF/LF _{nu}	146 ± 30	62 ± 11	6.9	0.01
LF/HF _{nu}	129 ± 28	250 ± 45	5.1	0.03

Values are means ± SE. HF, R-R interval spectral power at the high frequency (0.15–0.4 Hz); LF, R-R interval spectral power at the low frequency (0.05–0.15 Hz); Tot, total R-R interval spectral power (0.05–0.4 Hz); LF/HF, ratio indicating relative sympathetic predominance; HF/LF, ratio indicating relative parasympathetic predominance; HF_{nu}, normalized high frequency R-R interval spectral power; LF_{nu}, normalized low frequency R-R interval spectral power; HF/LF_{nu}, normalized ratio indicating relative parasympathetic predominance; LF/HF_{nu}, normalized ratio indicating relative sympathetic predominance.

between the two groups when data were expressed as absolute values. However, it is recommended that comparisons between spectral components also be made on data that have been normalized for the absolute value of the total variance of the signal (analogous to total power).¹⁵ HF_{nu} and the HF/LF_{nu} ratio (including the ratio expressed in absolute units) was higher, LF_{nu} and the LF/HF_{nu} ratio was lower in patients who died from their injuries compared with patients who lived (Table 3).

Figure 3 shows average spectral power for all 30 patients

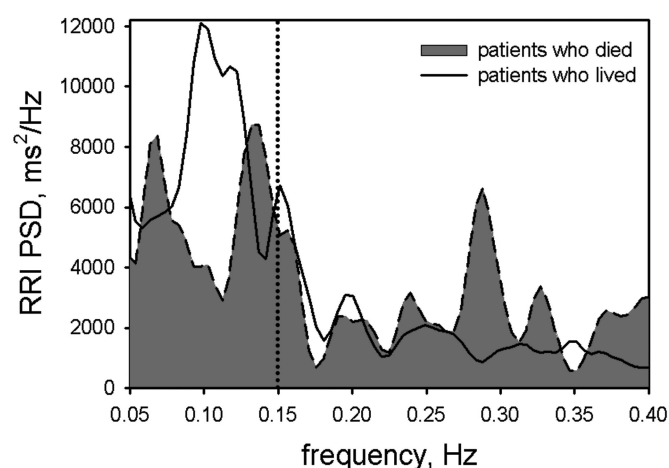
**Fig. 3.** Average R-R interval power spectral density (RRI PSD) is shown for 15 patients who lived (solid line) and 15 patients who died (broken line with red shading) traumatic injuries requiring transport to a level one trauma center; vertical dotted line denotes the demarcation of low-frequency (0.05–0.15 Hz) and high-frequency (0.15–0.4 Hz) spectral bands.

Table 4 Multivariate Summary

Effect Tested	Model Covariate(s)	Adjusted Group Means		Likelihood Ratio ($\chi^2_{HF/LF}$)	P value
		Died	Lived		
HF/LF	—	174	65	9.96	0.0016
HF/LF	Age	171	68	5.19	0.0227
HF/LF	RRI	167	72	7.06	0.007
HF/LF	GCS	152	87	1.96	0.1619
HF/LF	Age, RRI, GCS	132	108	0.43	0.487

Multivariate model with between group difference in HF/LF adjusted for variables that also indicated between group differences.

HF, R-R interval spectral power at the high frequency (0.15–0.4 Hz); LF, R-R interval spectral power at the low frequency (0.05–0.15 Hz); RRI, interbeat R-R interval; GCS, Glasgow Coma Scale score.

separated into those who lived and those who died. Figure 3 shows graphically the differences in R-R interval oscillations at low frequencies around 0.1 Hz and at high frequencies around 0.3 Hz.

The univariate analysis only suggests possible differences that may exist between subjects who die and those who survive. Such analysis does not account for the redundancies that exist between variables and the confounds that exist between groups. We determined that from all of the frequency-domain variables, HF/LF in absolute units accounts for the greatest amount of between group variance. Table 4 presents the results of a multivariate model in which the between group difference seen in HF/LF was adjusted for variables that also indicated between group differences (Tables 1 and 2). These covariates included age, GCS, and RRI. When HF/LF is adjusted for age or RRI, there is a slight reduction in HF/LF group means compared with the HF/LF univariate results. However, the HF/LF effect still explains approximately 20% of the between group variance when adjusted for either age or RRI. When HF/LF is adjusted for GCS, the between group variance accounted for by HF/LF is reduced to 6% and the *p* value associated with the HF/LF effect drops to 0.1619. When all three covariates are entered into the model simultaneously, the variance accounted for by the HF/LF effect and the associated *p* values are 1% and 0.4877, respectively. These results are shown in Table 4.

DISCUSSION

We assessed heart rate variability from electrocardiograms recorded in the prehospital environment from trauma patients who died to assess whether mortality is associated with estimates of autonomic function. The primary new findings are: 1) analysis of heart rate variability in prehospital trauma patients provides insight into adequacy of autonomic compensation and survival after trauma; and 2) patients who survive their injuries have higher pulse pressures and maintain high sympathetic modulation, whereas patients who die have low pulse pressures, withdraw their sympathetic tone and display inappropriate parasympathetic neural predomi-

nance as estimated from analysis of heart rate variability. However, heart rate variability analysis contributes no additional predictive value in a multivariate model when it is covaried with GCS scores. Our results suggest that autonomic balance and pulse pressure are associated with mortality, and may provide important diagnostic and prognostic information to assist the first responder in on-site triage, remote triage, and evacuation priority in the absence of obtainable GCS scores.

Oscillations in heart-period intervals in humans separate into HF (0.15–0.4 Hz) and LF (0.05–0.15 Hz) bands.¹⁴ R-R interval oscillations at HF are abolished with vagal blockade,¹⁶ and so changes in R-R interval oscillations at HF represent primarily parasympathetic activity. Oscillations occurring at frequencies lower than respiration are blunted with vagal blockade but abolished with the combination of vagal and sympathetic blockade,¹⁶ and so LF R-R interval oscillations are modulated importantly by both parasympathetic and sympathetic activities. Because LF R-R interval rhythms are modulated by both branches of the autonomic nervous system, a vigorous debate has developed over the concept of sympathovagal balance (the ratio of LF/HF). Eckberg¹⁷ has argued that “calculations of sympathovagal balance may obscure rather than illuminate human physiology and pathophysiology,” and Malliani¹⁵ maintains that an indirect quantification of the relative contributions of sympathetic and parasympathetic modulation of sinus node rate may be obtained by calculating the ratios of LF and HF R-R interval spectral powers. Strong cases have been made both for¹⁵ and against¹⁷ the concept of sympathovagal balance, but when both LF and HF R-R interval powers are normalized to control for changes in total signal variance, LF_{nu} increases consistently, and HF_{nu} decreases consistently with maneuvers that increase sympathetic and decrease parasympathetic neural activities.¹⁸ In trauma care, the argument over whether spectral components of cardiac interbeat intervals track absolute activities of autonomic nerves is moot if interpretations of such spectral components give insights into patient outcome.

Compensations for traumatic injuries with consequent reductions of central blood volume include increased heart rate and peripheral vascular resistance. These autonomic compensations are mediated by withdrawal of parasympathetic and activation of sympathetic efferent neural traffic to the heart and vasculature. Controlled experimental hemorrhage in animals has revealed two primary phases of autonomic compensation: 1) sympathoexcitation, resulting in maintenance of arterial pressure and central organ perfusion by vasoconstriction; and 2) pronounced sympathoinhibition, resulting in vasodilation, bradycardia, and eventual cardiovascular collapse.¹⁹ Such phases are consistent with the observations of Barcroft and coworkers,²⁰ who demonstrated in a seminal study that circulatory collapse due to hemorrhage occurs in conjunction with sudden drops of peripheral resistance. We²¹ and others^{22,23} have reported previously that

during induced hypotension, peripheral resistance falls consequent to abrupt withdraw of sympathetic traffic. In humans undergoing simulated hemorrhage with lower body negative pressure^{21,23} or induced hypovolemia with passive head-up tilt and nitroprusside infusion,²² arterial pressures were maintained through sympathoexcitation up to the point where further increases in sympathetic activity were not possible. When subjects reached their limits for sympathetic activation, they experienced profound acute reductions of arterial pressure in conjunction with total withdrawal of sympathetic traffic (measured directly from the peroneal nerve with microneurography).^{21–23} Results from such controlled laboratory experiments suggest that maintenance of robust sympathetic nerve traffic is a prerequisite for maintaining compensated hemodynamics during hemorrhage.

However, it is not feasible to record directly and continuously from a sympathetic nerve in patients during either transport to a hospital or during prolonged observation in a hospital. Moreover, direct measurements from the vagus nerve have not been made in humans, but it may be possible to estimate relative parasympathetic and sympathetic predominance non-invasively by analyzing heart rate variability. Low total power (an estimate of overall autonomic tone), and high HF/LF (an estimate of parasympathetic predominance), were found to be associated with mortality in 742 patients monitored over the course of 6 months in a surgical ICU.⁷ Based on these results obtained primarily from stable patients, we hypothesized that power spectral analysis might also be of benefit in evaluating patients and providing prognoses in a prehospital scenario where patients may not be stable. Data presented in Table 2 highlight the lack of difference in heart rates, SpO₂ (in a small number of patients) or global measures of heart rate variability calculated in the time domain. The primary benefit of frequency domain over time domain analysis is the capacity to separate variabilities into frequency components that are related to physiologic processes. Normalized frequency bands and the autonomic ratios suggest significantly greater parasympathetic and lesser sympathetic predominance in patients who died versus patients who survived (Table 3). Our results are consistent with previous reports of sympathetic withdrawal and associated hypotension during simulated hemorrhage^{21,23} and induced hypotension,²² and are in agreement with the suggestion that mortal outcomes in ICU patients are associated with high parasympathetic and low sympathetic neural tone.^{6,7}

Patients who died were clearly identified by the flight medics as critically ill, as evidenced by an increased intubation rate and decreased GCS. These experienced providers recognized that these casualties were severely injured and required rapid evacuation, coupled with immediate life saving interventions. It is commonly recognized that young trauma patients can compensate for an extended period of time before rapidly decompensating. The inexperienced provider, or one caring for overwhelming mass casualty patients, may not recognize the precarious patient with a narrowed

pulse pressure that is moments away from cardiovascular collapse. The value of the results presented in this report is in the potential to deliver early indicators of injury severity, perhaps even from a remote location before the arrival of a first responder. Heart rates, SpO₂, and blood pressures are commonly recorded by the medical monitors that are placed in emergency vehicles and aircraft. However, our data suggest that these vital signs fail to provide a first responder with early adequate information as to whether a bleeding patient is progressing toward cardiovascular collapse that could lead, ultimately, to hemorrhagic shock and death.²⁴

In the present study, heart rates, SpO₂, and arterial pressures were not different between the two patient populations but pulse pressures were lower in patients who died compared with patients who lived. We speculate, but cannot prove, that changes of pulse pressure track changes of central blood volume. In a recent study, Leonetti et al.²⁵ found that both stroke volume and pulse pressure correlated closely with blood loss after phlebotomy therapy of approximately 350 mL. Although the speculation that changes of pulse pressure track changes of blood volume requires confirmation with animal models of controlled hemorrhage, we suggest that automated calculation of pulse pressure rather than presenting a mean arterial pressure may provide the first responder with information on primary volume status after injury rather than information pertaining to a secondary response to hemorrhage.

Data presented in this report, and those of others,^{6–8} also suggest that important information regarding the integrity and adequacy of autonomic neural function may be contained in components of heart rate variability. However, when estimates of autonomic function are adjusted for injury severity as quantified by GCS scores, such estimates may not provide the first responder with any additional useful information (Table 4). We propose that the utility of using frequency-domain analysis in prehospital trauma care may be specific for remote triage or other conditions where visual inspection or palpation of a casualty may not be possible. We also stress that there is at least one limitation to using heart rate variability analysis as a diagnostic tool in the prehospital patient, and that is the inability to obtain real-time spectral estimates from clean ECG signals. In their studies of patients with severe brain injuries, Baillard et al.⁸ collected ECGs under stable conditions in an ICU, insuring clean signals with readily identifiable R-wave fiducial points. It was possible then to develop algorithms to provide R–R interval spectral components in real time, a prerequisite for monitoring and interpreting changes in heart rate variability from some stable baseline value.⁸ In the present study, ECGs collected from the ProPac 206EL onboard Life Flight helicopters were, as expected, consistently noisy and required extensive manual filtering and postprocessing before we could determine with confidence R-wave fiducial points (Fig. 1). To investigate further the possibility of using frequency domain analysis of R–R intervals as a diagnostic and prognostic tool for the first

responder in real time, portable field vital sign monitoring devices must output cleaner ECG signals with readily identifiable R-waves and have built in data analysis capability.

A second limitation to the current study is the small number of patients compared. We recognize and stress that clinical decisions based on heart rate variability analysis should derive from robust samples of patients with appropriate statistical controls. Until limitations associated with technical issues and small sample sizes are addressed, our preliminary but unique observations only suggest at this time a reasonable hypothesis that should be explored further. Results of logistic regression analysis showed that frequency domain results are confounded by GCS scores. In future experiments, survivors should be compared with nonsurvivors for patients who have the same GCS score. Matching patients for GCS scores is necessary to determine whether heart rate variability analysis is predictive of, rather than simply associated with, mortality.

Based on frequency domain analysis of R-R intervals from data collected en route to a hospital, trauma patients who die from hemorrhagic shock increase their parasympathetic and decrease their sympathetic predominance compared with patients who survive their injuries. Although we concede that these results must be confirmed with larger patient populations, our results are consistent with reports that hemodynamic instability during experimentally-induced hypovolemia is associated with sympathetic neural withdrawal, and also with reports that mortality in ICU patients is associated with high parasympathetic and low sympathetic autonomic tone. Such autonomic responses occur in conjunction with significantly lower pulse pressures in patients who die, suggesting that pulse pressure may provide the first responder with a more accurate assessment of blood loss than arterial pressure alone. In the absence of obtainable GCS scores, analysis of heart rate variability represents a potential new approach to remote triage. Future devices incorporating real-time frequency domain analysis of R-R intervals and continuous estimates of pulse pressure could be constructed that would assist the first responder in identifying those casualties that require triage, evacuation, and intervention priority.

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EDITORIAL COMMENT

In this issue of the *Journal of Trauma*, Cooke and colleagues report their preliminary observations of prehospital physiologic variability in 15 seriously injured patients who died and 15 matched survivors. They performed retrospective analysis of continuous electrocardiographic traces that were acquired and stored in transport monitors. The authors assessed generally accepted time-domain (such as standard deviation) and frequency-domain (such as high- and low-frequency power) statistics. The major finding of the study related to different high- and low-frequency power ratios in patients who died compared with patients who survived.

What is important about this study is its attempt to describe the dynamics of what Samuel V. Gross famously described as the “rude unhinging of the machinery of life” in the prehospital setting of traumatic shock. In contrast to complementary reports that focus on the cardiac state after substantial resuscitation (for example, in the intensive care unit), the present study explores endogenous responses during the earliest phases of emergency care.

The data, which reflect comparatively small numbers of patients, suggest that the ratio of high-frequency (HF) to low-frequency (LF) power is different among patients who die compared with patients who survive. High HF/LF ratios were associated with mortality. The authors follow conventional wisdom, interpreting a high HF/LF ratio as an autonomic state in which parasympathetic activity predominates over sympathetic tone. In contrast, survivors had a lower HF/LF ratio, which is commonly interpreted as a robust sympathetic response. Put differently, the patients who died appeared to have exhausted the sympathetic arm of the autonomic nervous system. Such sympathetic exhaustion has been suggested by others to represent a preterminal condition. Indeed, the authors’ own analysis suggests that a high HF/LF

ratio adds little to a low Glasgow Coma Scale score, the latter also predicting death.

What, then, is the potential clinical value of HF/LF measures? First, they can be made continuously. Second, they do not require a trained observer for assessment, nor should they be subject to interrater variability. Third, with modern telemetry, they could be obtained remotely and simultaneously in large numbers of patients or potential patients, such as warfighters on the battlefield. In mass casualty situations, such measures could conceivably be used to triage victims.

Implementation and deployment of technology for such measures as clinical routine would have to overcome significant technical hurdles (the power spectral analysis that is used to generate the HF/LF measure is sensitive to artifact) and demonstrate its value in much larger studies. There are challenges related to the influence of chronic illnesses and medications on the range of normal values for HF/LF ratios. There are no population based studies of stress-related variation in HF/LF that yet inform us as to the presence or absence of heritable factors that might affect HF/LF. Put simply, there is a great deal to learn about how this metric might perform as a predictor in a larger and more heterogeneous population.

Perhaps the most intriguing aspect of the data is the way it informs the basic physiologic sciences. The “rude unhinging” now appears to be nonrandom: Cooke and colleagues’ data hint that death has a specific dynamic, a dynamic with a time signature that can be extracted from conventional physiologic monitoring. If this notion is correct—if the beginning of the “death spiral” can be detected before it is apparent to an observer or manifests in vital signs—then decompensation should be identifiable (and hopefully remediable) before complete physiologic collapse becomes both inevitable and irreversible.

Timothy G. Buchman

*Washington University School of Medicine
Seattle, WA*